

### REMARKS

Upon entry of the above amendment, claims 1-4, 9, 12, and 14-26 will be pending in this application, claims 5-8, 10, 11, and 13 having been canceled and new claims 14-26 added. Applicants have amended claims 1, 4, 9 and 12. Support for the amendments and new claims can be found throughout the specification and claims as filed, e.g., at page 3, lines 18-21; page 4, line 31, to page 5, line 10; page 5, lines 26-29; page 6, lines 1-8; page 6, lines 32-33; page 18, line 29, to page 19, line 4; and page 22, lines 3-8. The amendment to the specification corrects an obvious error in the translated specification. No new matter has been added.

### Information Disclosure Statement

Applicants request that the Examiner consider the references submitted with the Information Disclosure Statement filed June 26, 2007, and return an initialed Form PTO-1449 to applicants to indicate this has been done.

### Rejections Under 35 U.S.C. § 102

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Hansen (Hansen et al., Proc. Natl. Acad. Sci. USA, 98:12659-64, 2001). Claims 5-7 have been canceled without prejudice, mooted the rejection with respect to these claims.

To anticipate a claim, a reference must teach every element of the claim. See MPEP § 2131. The amendment to claim 1 makes it clear that the claim requires a step of isolating a single lesional tissue-infiltrating B cell. As indicated in the specification at page 6, isolation of a single B cell makes it possible to obtain sequences encoding both the heavy chain and the light chain of a naturally occurring antibody from a single B cell. Hansen does not teach or suggest such a step. Rather, Hansen teaches isolating total cellular RNA from heterogeneous tissue containing multiple tumor-infiltrating B cells. See p. 12660, col. 1, "V(D)J Analysis and Library Construction" and p. 12660, col. 2, "Reverse Transcriptase-PCR Amplification of Ig V(D)J Segments . . ." In order to obtain intact antibodies that bound to tumor-related antigens, Hansen needed to prepare a library of randomly associated antibody heavy and light chains prepared

from the total cellular RNA. See p. 12660, col. 1, “V(D)J Analysis and Library Construction” and p. 12661, col. 1-2, “Selection of Antibodies from Phage Display Libraries Generated from the Tumor-Infiltrating Lymphoplasmacytic Cells of Patients with MCB.” Because Hansen does not teach a step of isolating a single lesional tissue-infiltrating B cell, Hansen does not anticipate claim 1 or any claim that depends therefrom, i.e., claims 2-4 and 14-26. Claims 10 and 11 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Punt (Punt et al., Cancer Immunol. Immunother., 38:225-232, 1994). As claims 10 and 11 have been canceled without prejudice, the rejection of those claims is moot.

#### Rejection Under 35 U.S.C. § 103

Claims 1-13 were rejected as allegedly unpatentable over Hansen in view of Larrick (Larrick et al., Immunol. Rev., 130:69-85, 1992). To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. See MPEP § 2143.03. Each of the independent claims, claims 1 and 9, has been amended to specify a step of isolating a single B cell from a lesional tissue. As indicated above, Hansen does not teach or suggest such a step. Larrick also does not teach or suggest a step of isolating a lesional tissue-infiltrating B cell (nor does the Office action allege such). Because neither Hansen nor Larrick teaches or suggests a step of isolating a single lesional tissue-infiltrating B cell, and provides no motivation to do so, these references, even in combination, do not support an obviousness rejection of any of the claims.

In addition, the claimed methods are highly advantageous in that the isolation of infiltrating B cells increases the possibility of obtaining specific antibodies against lesional (e.g., cancer) tissues. This advantageous effect is demonstrated in, for example, Example 3 (page 22, lines 10-12 of the specification, and Figs. 3 and 4), which shows that a number of clones obtained from isolated B cells using a presently claimed method had almost the same amino acid sequences of heavy and light chain variable regions.

Applicants request withdrawal of the rejection.

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Serial No. : 10/535,764  
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Page : 8 of 8

Attorney's Docket No.: 14875-144US1 / C1-A0230P-US

### Conclusion

Applicants submit that all claims are in condition for allowance, which action is respectfully requested.

This reply is being submitted with a petition for extension of time and the required fee. Please apply any other required charges or credits to deposit account 06-1050, referencing Attorney Docket No. 14875-144US1.

Respectfully submitted,

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